REMARKS

Claims 11, 13-14, 18-20, 33-41, 44, 50-55, 57-58, and 60 are pending in the present application. Claims 12, 15, 42-43, 56, and 59 have been canceled without prejudice or disclaimer. Claims 18 and 37 have been amended to further define the subject matter recited therein. Claims 37-38 and 40 have been amended to correct dependency. Applicants hereby reserve the right to pursue any one or more of the cancelled claims in a continuation or divisional application.

No new matter has been added.

In view of the following, further and favorable consideration is respectfully requested.

1. Rejection of claims 11, 12, and 18 under 35 U.S.C. §112

The Official Action states that claims 11, 12, and 18 are rejected under 35 U.S.C. § 112 reciting new matter.

In particular, the Official Action states the following:

> Applicant's recitation of "wherein the microsphere does not comprise an enteric coating" in instant claims 11, 12 & 18 presents new matter since there is lack of support for this limitation in the present specification. While the limitation "the acid-labile active compound does not have to be protected by an enteric coating" is supported by the instant disclosure at page 3, first paragraph, the limitation "wherein the microsphere does not comprise an enteric coating" is not supported by the instant specification. Examiner requests clarification as to where in the instant specification support for the new limitation can be found.

RESPONSE

Applicants respectfully submit that claim 12 has been cancelled without prejudice or disclaimer of the subject matter contained therein, rendering the rejection of this claim moot.

Applicants respectfully traverse this rejection of presently pending claims 11 and 18 under 35 U.S.C. § 112.

Applicants respectfully submit that the present limitation that "the microsphere does not comprise an enteric coating," as recited present claims 11 and 18, is not new matter within the meaning of 35 USC § 112.

Applicants submit the skilled artisan would understand the teaching of the specification as including the limitation that the microsphere does not comprise an enteric coating. Specifically, the specification teaches that neither the individual active compound, i.e, that comprising a matrix, which comprises a microsphere, nor the acid-labile active compound, require enteric coating. *See* the specification at page 3, first paragraph, and the paragraph bridging pages 10 and 11. Accordingly, it would follow that as an integral structure of the individual active compound, the microsphere would also be precluded from requiring enteric coating.

Furthermore, as admitted by the Examiner, "the acid-labile active compound does not have to be protected by an enteric coating." In this regard, Applicants respectfully note that in one embodiment the present specification describes the active compound units as microspheres. Specifically, as described at page 4 of the present specification:

> The multiple individual active compound units (also described in preparations below) within the meaning of the invention are multiple individual units, in which at least one active compound particle is present in a matrix made of a mixture comprising at least one fatty alcohol and at least one solid paraffin.... Preferably the active compound units are microspheres. *See* the present specification at page 4, paragraph 3.

Again, as the acid-labile active compound would not have to be enteric coated, it would follow that the microsphere would not have to be enteric coated. Applicants respectfully submit that upon a cursory reading of the specification a skilled artisan would realize, and understand, that the microsphere does not comprise an enteric coating.

Therefore, Applicants submit that the limitation the present limitation that "the microsphere does not comprise an enteric coating," as recited claims 11 and 18, is not new matter within the meaning of 35 USC § 112. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 11 and 18.

2. Rejection of claims 11-15, 18-20, 33-43, and 48-60 under 35 U.S.C. §103(a)

The Official Action states that claims 11-15, 18-20, 33-43, and 48-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inagi et al. (U.S. Patent No. 6,582,720 in view of Benton et al. (U.S. Pat. No. 4,876,094).

In particular, the Official Action states the following:

> The instant invention is drawn to an oral solid active compound unit comprising a microsphere, the microsphere comprising: a matrix comprising a mixture of at least one fatty alcohol and at least one solid paraffin; and an acid-labile active compound, selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, wherein said acid-labile active compound is present in said matrix, and wherein the microsphere does not comprise an enteric coating.
>
> The instant invention is also drawn to an oral solid active compound unit comprising a microsphere, the microsphere comprising: a matrix comprising a mixture of at least one fatty acid ester or at least one triglyceride, and at least one solid paraffin; and an acid-labile active compound, selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, wherein said acid-labile active compound is present in said

matrix and wherein the microsphere does not comprise an enteric coating.

Inagi et al. (120) teach a gastric and/or duodenal pharmaceutical composition which comprises a medicament acting at the stomach and/or duodenum and one or more ingredients selected from water insoluble polymers, polyglycerin fatty acid esters, lipids and waxes (see column 1, line 53 – col. 2, line 9 and Abstract). Inagi et al. teach that the composition may be a matrix containing medicament, necessary additives and various water-insoluble ingredients as a mixture (col. 4, lines 60-67).

Suitable Polyglycerin fatty acid esters are disclosed at column 3, lines 14-32).

Lipids are disclosed and include higher fatty acids and salts thereof, higher alcohols and fatty acid glycerin esters and those of the wax include waxes and hydrocarbons (col. 3, lines 3335). Examples of higher alcohols taught include stearyl alcohol and cetyl alcohol (col. 3, lines 35-39). Triglycerides are also disclosed (col. 3, lines 40-42). Waxes disclosed include paraffin wax (col. 3, lines 42-44). These ingredients, namely, water-insoluble polymers, polyglycerin fatty acid esters, lipids and waxes may be used singly or in combination (col. 3, lines 45-48).

Suitable medicaments disclosed include proton pump inhibitors (PPIs) such as omeprazole and lansoprazole, which can be used in amounts of 0.01 to 95% (col. 3, line 60 – col. 4, line 30). Moreover, with regards to amounts, it is deemed obvious to determine suitable amounts through the use of routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art. Furthermore, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The particle size of the pharmaceutical composition is within a range of 30 to 300 gm (col. 5, lines 20-24).

Excipients are included and taught at column 4, lines 39-56.

A process for the preparation of a matrix is disclosed at col. 5, lines 39-50.

Inagi et al. do not teach a process that involves prilling a solution or dispersion to obtain drops.
Benton et al. (`094) teach a dual coated dosage formulation comprising dosage form cores such as matrix beads/microspheres containing a therapeutically active compound over which there are applied two unique coatings (see reference column 1, line 55 — col. 2, line 20). The controlled release microspheres/matrix beads can be prepared by microencapsulation processes including prilling, pan coating, granulation fluidization processes and other processes (col. 5, lines 60-66).

Ingestible materials taught include waxes such as paraffin, higher fatty acids, esters of fatty acids such as glyceryl tristearate, cetyl palmitate, diglycol stearate, glyceryl myristate, triethylene glycol monostearate, higher fatty alcohols such as cetyl alcohol and stearyl alcohol and high molecular weight polyethylene glycols and mixtures thereof (col. 3, lines 23-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate processes, such as prilling, as taught by Benton et al. within the matrix formulations of Inagi et al. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Benton et al. teach a dosage formulation comprising micropsheres that are produced by effective microencapsulation processes, which include prilling. The expected result would be an improved and highly effective pharmaceutical composition for treating disorders and conditions.

RESPONSE

Applicants respectfully submit that claims 12, 15, 42-43, 56, and 59 have been cancelled without prejudice or disclaimer of the subject matter contained therein, rendering the rejection of these claims moot.

Applicants traverse the rejection of presently pending claims 11, 13-14, 18-20, 33-41, 44, 50-55, 57-58, and 60 under 35 U.S.C. § 103(a) because a *prima facie* case of obviousness has not been established.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, *supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

From the outset, Applicants note that Inagi et al. is not prior art within the meaning of 35 U.S.C. 103(a) because it is not prior art under the pertinent sections of 35 U.S.C. 102, i.e. 35 U.S.C. §§ 102(a), 102(b), and/or 102(e). Briefly, the present application is a national phase application of an International Application that claims priority to a European Patent Application. The present application was filed as a national phase application in the US on December 4, 2001. The International Application was filed on May 31, 2000. The European Patent Application, to which each of these applications claims priority, was filed on June 7, 1999. Accordingly, under US law, **the present application has a priority date of June 7, 1999**.

Similarly, the Inagi et al. reference is a patent granted on a national phase application of an International Application. However, Inagi et al. claims priority to two Japanese Patent Applications. Inagi et al. was filed in the US on September 7, 2000. The International Application from which Inagi et al. matured was filed on March 17, 1998 and published on September 30, 1999. One of the Japanese applications from which Inagi et al. claims priority was filed on March 20, 1999 and published on September 24, 1999. The other Japanese application from which Inagi et al. claims priority was filed on March 20, 1999 and published on October 5, 1999.

Regarding § 102(a), there is not sufficient evidence to show that Inagi et al. was known or used in the US prior to invention of the presently claimed subject matter. Additionally, Inagi et al. was not patented or published anywhere prior to the priority date of the present application.

With regard to § 102(b), Inagi et al. was not patented or published more than one year before the present application date. As noted above, the present application has an earliest effective priority date of June 7, 1999. In contrast, none of the Inagi et al. patents or published applications published before June 7, 1999.

Finally, regarding 102(e), because the International Application from which Inagi et al. matured was filed prior to November 29, 2000, its 102(e) prior art date is its 35 U.S.C. § 371 (c)(1), (2), (4) US filing date, i.e. September 7, 2000. Therefore, since the presently pending claims validly claim priority to the European Patent Application filed on June 7, 1999, this rejection is overcome simply by pointing out to the Examiner that the Inagi et al. reference does not qualify as prior art against the present application.

Furthermore, Applicants submit that a *prima facie* case of obviousness has not been established because Benton et al. does not teach or suggest each and every limitation of the presently pending claims as required by *In re Wilson*.

Benton et al. is directed to an acidic, liquid dosage formulation where the active compound is contained in the matrix of a dual-coated microsphere. Benton et al. requires the dual-coating in order to prevent release of the active compound into the acidic liquid carrier. *See* Benton *et al.* at col. 12, lines 60-68; and col. 16, lines 11-18. Benton et al. further requires that the acidic carrier comprise a sugar-based acidic liquid in order to achieve restricted release of the active compound. *See* Benton et al. at col. 13, lines 46-51, and claim 1. Benton et al. describes active compounds at col. 6, lines 43-50.

Additionally, Benton et al. describes suitable microsphere matrix components/binders at col. 3, lines 5-46. Benton et al. asserts that binders can include paraffin; higher fatty acids; esters of fatty acids such as glyceryl tristearate, cetyl palmitate, and diglycol stearate; higher fatty alcohols such as cetyl alcohol and stearyl alcohol; and high molecular weight polyethylene glycols.

Independent claim 11 is directed to an oral solid active compound unit comprising a microsphere, the microsphere comprising: a matrix comprising a mixture of at least one fatty alcohol and at least one solid paraffin; and an acid-labile active compound selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, wherein said acid-labile active compound is present in said matrix, and wherein the microsphere does not comprise an enteric coating.

Claim 18 is directed to a process for the production of an oral solid active compound unit in the form of a microsphere comprising an acid-labile active compound, where the acid-labile active compound is selected from the group consisting of an acid-labile proton pump inhibitor, a salt of an acid-labile proton pump inhibitor with a base, and a hydrate of a salt of an acid-labile proton pump inhibitor with a base, and is present in the microsphere in a matrix made of a mixture comprising at least one fatty alcohol and at least one solid paraffin, comprising the following steps: a. preparing a solution or dispersion of the acid-labile active compound in the fatty alcohol and paraffin; b. prilling the solution or dispersion prepared in step (a) and obtaining drops of the solution or dispersion;

and c. solidifying the drops obtained in step (b) in a suitable medium, wherein the microsphere does not comprise an enteric coating. All remaining pending claims depend, either directly or indirectly from claims 11 and 18.

Benton et al. do not teach or suggest all of the elements of independent claims 11 and 18 because Benton et al. do not teach or suggest an oral solid active compound unit comprising a microsphere wherein either the microsphere, or the oral solid active compound unit, does not comprise an enteric coating. Further, Benton et al. teach liquid dosage formulations. Moreover, Benton et al. do not teach solid formulations as recited in the presently pending claims. Additionally, Benton et al. do not teach an active compound being an acid-labile proton pump inhibitor or a salt of an acid-labile proton pump inhibitor with a base or a hydrate of a salt of an acid-labile proton pump inhibitor with a base.

As Inagi et al. is not prior art within the meaning of 35 U.S.C. § 103, and each and every element of the presently pending claims are not taught or suggested by Benton et al., Applicants submit that a *prima facie* case of obviousness has not been established. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection of presently pending claims 11, 13-14, 18-20, 33-41, 44, 50-55, 57-58, and 60.

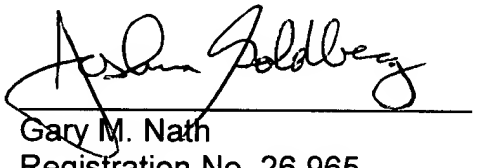
Conclusion

In view of the foregoing, Applicants submit that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



Gary M. Nath
Registration No. 26,965
Joshua B. Goldberg
Registration No. 44,126
Ari G. Zytcer
Registration No. 57,474
Customer No. 34375

Date: July 24, 2007

THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314
Tel: (703) 548-NATH
Fax: (703) 683-8396